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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,116	07/03/2003	Colin M. Tice	A01386-US	3335

7590 05/30/2006

RheoGene, Inc.
2650 Eisenhower Avenue
Norristown, PA 19403

EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 05/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,116	TICE ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07/03/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the invention of Group IV, drawn to a method of modulating the expression of a target gene using the compound of formula I in the reply filed on 03/13/2006 is acknowledged. The traversal is on the ground(s) that the methods of Groups IV-VII all relate to the use of the compounds as ligands for the same inducible gene expression system. Applicants argue that examination of the methods of Groups IV-VI involves determination of the novelty of the claimed ligands, and therefore the searches for the methods of Groups IV-VI are coextensive and would not impose a serious burden to the Examiner. This is found persuasive for the methods of Groups V and VI and therefore, the restriction requirement between the inventions of Groups IV-VI is withdrawn. However, the restriction between Groups IV-VI and VII is maintained for the reasons of record in the restriction requirement of 01/13/2006. To wit, in addition to meeting the requirements of restriction under 35 U.S.C. 121 and 372, each of the groups has different structural and functional considerations which are non-coextensive, and lead to a serious burden to the Examiner to search and examine these groups together. Applicants assert that the search is not undue. However, the invention of Group VII uses different steps and compositions as compared to the inventions of Groups IV-VI, such as introducing into a host cell three different expression cassettes. Therefore they require separate and non-coextensive searches in the patent and non-patent literature. Hence, restriction is proper. Additionally, the species election between the compounds of formulae I-III is proper because they are

drawn to compounds with distinct structures that can be made and used independent of each other. Because of their distinct structures, the compounds require different searches in the patent and non-patent literature. Therefore, a search and examination of anything more than one of the designated species is a burden to the Examiner. The restriction requirement between the inventions of Groups IV-VI and VII and the species election requirement are still deemed proper and are therefore made FINAL.

Claims 1-5 and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 6-17 are pending.

Note: Change in Art Unit and SPE

The Examiner of record is now Ileana Popa, Art Unit 1633. Therefore, future correspondence should reflect such changes. Also, at the end of the Action is the information regarding the SPE and the Art Unit.

Specification

2. The disclosure is objected to because of the following informalities: Applicants claim benefit of U.S. Application No. 60/393,960, filed on 07/05/2002. The first paragraph of the specification must include the information regarding the claimed priority.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 6-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martinez et al. (Mol Gen Genet, 1999, 261: 546-552), in view of both Dhadialla et al. (Annu Rev Entomol, 1998, 43: 545-569) and Saez et al. (Proc Natl Acad Sci USA, 2000, 97: 14512-14517), as evidenced by Guan et al. (Journal of Combinatorial Chemistry, 2000, 2: 297-300) and Michelotti et al. (U.S. Patent No. 5,304,572).

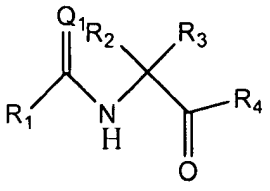
Martinez et al. teach plant cells co-transformed with (i) an ecdysone receptor chimera, wherein the receptor chimera comprises the ligand-binding domain of insect ecdysone receptor (i.e., a Group H nuclear receptor ligand binding domain) fused to the transactivation and DNA-binding domains of the glucocorticoid receptor (GR) (Abstract, p. 547, column 1, first paragraph), and (ii) a construct comprising six copies of the glucocorticoid response element (i.e., a response element capable of binding to the GR DNA binding domain), a promoter that is activated by the GR transactivation domain, and a target gene encoding for β-glucuronidase (GUS), i.e., a polypeptide (p. 547, column 2, last paragraph). Martinez et al. teach modulation of the expression of the target gene by contacting the transformed cells with non-steroidal ecdysone agonists (Abstract, p. 547, column 1, second paragraph, p. 549, Fig. 3 and 4). Martinez et al. also teach using the ecdysone system to modulate gene expression in transgenic plants

(p. 550, column 2). Martinez et al. teach that a large range of synthetic ecdysone agonists that are compatible with agricultural can be used to induce gene expression from various chimeric ecdysone promoters (p. 547, column 1, second paragraph). However, Martinez et al. do not specifically teach modulation of gene expression by using a compound having the claimed formula I, or modulating gene expression in a subject. Dhadialla et al. teach DTBHIB, a non-steroidal ecdysone agonist used as a pesticide, with a structure similar to the claimed formula I (see below). Dhadialla et al. do not teach using this compound to modulate gene expression in a host cell or in a subject. However, Saez et al. teach that non-steroidal ecdysone analogs, generally used as pesticides, can also be used as activators of the ecdysone system in mammalian cells and transgenic animals (Abstract, p. 14512, column 2, third paragraph). Moreover, at the time the invention was made, the claimed compound was already known and used as a pesticide (see Michelotti et al., column 2, and also formula below). Although Michelotti et al. do not teach their compound as an ecdysone analog, its structure is similar to the compound of Dhadialla et al. (see below). Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to use the method of Martinez et al. with the compound of Michelotti et al., both *in vitro* and *in vivo*, with a reasonable expectation of success. Additionally, since the teachings of the prior art suggest that compounds having structures similar to the compound of Dhadialla et al. could be used as ecdysone analogs, it would have been obvious to one of skill in the art to use the compound of Dhadialla et al. as a central core to generate diverse substituted compounds similar to the compound of Michelotti et al., with a

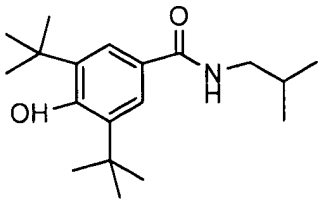
reasonable expectation of success. The following is a citation from MPEP:

> 2144.08 II. A.4.(c)
>
> (c) Consider the Teachings of Structural Similarity
> Consider any teachings of a "typical," "preferred," or "optimum" species or subgenus within the disclosed genus. If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214 ("Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."). The utility of such properties will normally provide some motivation to make the claimed species or subgenus. Id.
> In making an obviousness determination, Office personnel should consider the number of variables which must be selected or modified, and the nature and significance of the differences between the prior art and the claimed invention.

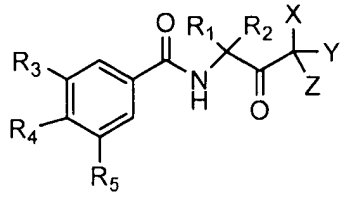
The motivation to use such diverse ecdysone analogs is provided by Saez et al. who teach the necessity of broadening the utility of the ecdysone-based gene modulation. The motivation to use the compounds *in vivo* is also provided by Saez et al., who teach the utility of modulating gene activity in transgenic animals for the discovery of new gene functions or therapeutics (p. 14512, column 1). One of skill in the art would have been expected to have a reasonable expectation of success in making and using such compounds because the art teaches that such compounds can be easily generated if the central core is known (see Guan et al.) and because Saez et al. teach that non-steroidal ecdysone analogs can be successfully used for modulating gene expression via the ecdysone system. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.



Claimed formula I, wherein R_1 can be substituted phenyl, and Q_1 can be O.



Dhadialla et al



Michelotti et al.

5. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa

JANET L. EPPS-FORD, PH.D.
PRIMARY EXAMINER